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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/782,596	02/19/2004	Chen W. Liaw	AREN-011CON(11.US12.CON)	5835

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EXAMINER	
LI, RUIXIANG	
ART UNIT	**PAPER NUMBER**
1646	

MAIL DATE	DELIVERY MODE
10/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/782,596	LIAW ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-8,21-26 and 28-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-8, 21-26, 28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 February 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/20/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/20/2007 has been entered.

The amendment filed on 02/20/2007 has been entered in full. Claims 5-8, 21-26 and 28-30 are pending and under consideration.

Withdrawn Objections and/or Rejections

The objection to claims 5, 7, 21, 24, and 28 for minor informalities is withdrawn in view of amended claims.

Information Disclosure Statement

The Information Disclosure Statement submitted on 08/20/2007 has been considered. An initialed copy is attached to this office action.

Drawings

The drawings, Fig. 3 and 5, filed on 02/20/2007 are accepted.

Claim Rejections Under 35 U.S.C. §101

(i). 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

(ii). Claims 5-8, 21-26, and 28-30 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 5-8, 21-26, and 28-30 are drawn to a method for identifying one or more candidate compounds as an agonist, partial agonist, or inverse agonist of a G protein-coupled receptor (GPCR) comprising the polypeptide of SEQ ID NO: 20 or a variant of thereof. The claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" context of use for the claimed invention which does not require further research.

The specification discloses the hARE-2 polypeptide of SEQ ID NO: 20, a putative GPCR, which shares 53% sequence homology to GPR27 (Table A, page 8) and that the hARE-2 polypeptide is expressed in the left and right cerebellum and in the substantia nigra (Table 27, page 27). Nonetheless, the specification fails to disclose the ligand of the putative GPCR, fails to provide any sufficient information or evidence on the biological functions or activities of the hARE-2 polypeptide of SEQ ID NO: 20, and fails to disclose a patentable utility for the claimed invention.

First, the invention lacks a well-established utility. A well-established utility is a specific, substantial, and creditable utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. The assertion that the hARE-2 polypeptide of SEQ ID NO: 20 has 53% sequence homology to GPR27 does not endow the hARE-2 polypeptide and the claimed invention with a specific and substantial utility due to the great diversity in structures and functions of the GPCR family (Ji et al., *J. Biol. Chem.* 273:17299-17302, 1998). The functions of a GPCR have to be determined experimentally. Therefore, even if the sequence analysis can place a GPCR into the GPCR family, such an assignment does not render a specific biological function and thus a well-established utility to the GPCR, as is the case here. It is noted that neither the instant disclosure nor the prior art teaches the specific biological functions of GPR27, which the hARE-2 polypeptide is compared with.

The state of the art is such that the biological functions of proteins are unpredictable solely based upon sequence homology. The prior art teaches that sequence-based methods for function prediction are inadequate (*Trends in Biotech* 18: 34-39, 2000). There are putative seven transmembrane molecules, which do not appear to be coupled to a G protein (Ji et al., *J. Biol. Chem.* 273:17299-17302, 1998; in particular, the 3rd paragraph of left column of page 17299). No art of record discloses or suggests any property or activity for the claimed molecules such that another non-asserted utility would be well-established for the claimed invention.

Secondly, the present invention does not have a specific and substantial utility, as exemplified below. The specification asserts, for example, that the human orphan GPCR can be used to screen candidate compounds as inverse agonists, agonists or partial agonists (see, e.g., page 15). These asserted utilities are not specific and substantial because they do not identify or reasonably confirm a "real world" context of use. The disclosure fails to identify the ligand and the biological functions of the hARE-2 polypeptide. Clearly, further research would be required to determine the functions of the hARE-2 polypeptide. See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966), noting "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

In summary, the present invention fails to satisfy the utility requirement under 35 U.S.C. 101.

(iii). Response to Applicants' argument

Applicants argue that the claimed method can be used to identify compounds that increase the "well-being" of substantia nigra cells and stave off or slow the progression of Pakinson's disease. This is not persuasive because the instant disclosure has not disclosed that the hARE-2 is linked to Parkinson's disease. Moreover, since the biological function of hARE-2 is not disclosed, the compound identified in the methods using hARE-2 does not have a specific and substantial utility. The use of compounds

identified in the method in increasing the "well-being" of substantial nigra cells is a "throw-away" utility.

Applicants argue that the claimed screening methods can be employed to identify compounds that can be employed in the study, diagnosis or monitoring of Parkinson's disease. This is not persuasive because the instant disclosure fails to disclose that an agonist, partial agonist, or inverse agonist of the GPCR of SEQ ID NO: 20 can be used for the diagnosis of Parkinson's disease. In addition, the use of a compound identified by the claimed method in the study of Parkinson's disease is considered a research utility and it does not represent a specific and substantial utility.

Applicants argue that the substantia niga-selective expression of hARE-2 makes hARE-2 conceptually no differ from a marker for any diseased cells. Applicants' argument has been fully considered, but is not deemed to be persuasive because the instant claims are drawn to a method for identifying one or more candidate compounds as an agonist, partial agonist, or inverse agonist of a G protein-coupled receptor (GPCR) comprising the polypeptide of SEQ ID NO: 20 or a variant of thereof. The determination of the utility of the claimed invention is based upon the utility of the compounds identified by the methods. Since the instant disclosure fails to provide a patentable utility for the compounds identified by the present methods, the instantly claimed methods do not have a specific and substantial utility.

Claim Rejections Under 35 U.S.C. §112, 1st Paragraph due to lack of utility

Claims 5-8, 21-26, and 28-30 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicants argument regarding the utility of the claimed invention has been fully considered, but is not deemed to be persuasive for the reasons set forth in the preceding section.

Claim Rejections under 35 USC § 112, 1st paragraph, Written Description

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 28-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics,

structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 28-30 are drawn to a method for identifying one or more candidate compounds as an agonist, partial agonist, or inverse agonist of a G protein-coupled receptor comprising the polypeptide of SEQ ID NO: 20 or an endogenous version thereof which is encoded by a polynucleotide that hybridizes under stringent conditions to the complement of SEQ ID NO: 19, wherein said stringent conditions comprises a wash at 65 ^{0}C in 0.1xSSC. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature.

The instant disclosure of an isolated polypeptide of SEQ ID NO: 20 and its encoding nucleic acid molecule set forth in SEQ ID NO: 19 does not adequately support the scope of the genus recited in the claims, which encompasses a substantial variety of variants of the polypeptide of SEQ ID NO: 20. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). While disclosing the amino acid sequence of SEQ ID NO: 20, the instant disclosure fails to provide sufficient description information,

such as definitive structural or functional features of the genus of polypeptides recited in the claims. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the instant disclosure fails to describe the features of the endogenous version of the polypeptide of SEQ ID NO: 20. Finally, the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed polypeptides as being identical to those instantly recited.

Due to the breadth of the claimed genus and lack of the definitive structural or functional features of the recited genus and failure to describe the feature of endogenous version of the polypeptide of SEQ ID NO: 20, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the recited genus and thus the instantly claimed methods.

(iii). Response to Applicants' argument

Applicants argue that the GPCRs recited in the rejected claims are naturally produced and encoded by a polynucleotide that hybridizes to SEQ ID NO: 19. Applicants argue that given this, one of skill in the art would not expect the incredibly broad range of variation the Examiner seems to read into the claims.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. First, the claims do not require that the polypeptides recited in the claims possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature. Secondly, the claims recite "stringent conditions", however, only the washing conditions are given, which would yield structurally and functionally unrelated polypeptides. Furthermore, the mere disclosure of SEQ ID NO: 20 is not sufficient to support the genus of recited in the claims. Finally, the specification fails to describe the features of the endogenous version of the polypeptide of SEQ ID NO: 20 so as to one of skill in the art can readily recognize it.

Claim Rejections under 35 USC § 112, 2nd paragraph

(i). The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(ii). Claims 5-8, 21-26, and 28-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 5-8, 21-26, and 28-30 are indefinite for the following reasons:

(1). Claims 5-8, 21-26, and 28-30 recite "(b) measure the ability of the compound that inhibit or stimulate said receptor". It is unclear what activity of said receptor is intended to be measured, rendering the claims indefinite.

Applicants argue that given the specification and the teachings of the prior art, one of skill in the art would have no trouble understanding what is meant by the phrase "measuring the ability of the compound or compounds to inhibit or stimulate said receptor". Applicants argue that given the discussion in the Background section of this patent application, one of skill in the art would readily understand that the phrase means coupling to a G protein or a signal that is transduced by the receptor. This is not found to be persuasive because the claims are required to particularly point out and distinctly claim the subject matter which applicant regards as the invention under 35 U.S.C. 112, second paragraph. In this case, neither the prior art nor the specification provides an unambiguous definition for the term and the claims fail to point out and distinctly claim the subject matter.

(2). The steps of the methods of claims 5-8, 21-26, and 28-30 do not necessarily achieve the goal set forth in the claim preamble. The amended claims now recite "(c) identifying the compound or compounds that ***inhibit or stimulate*** said receptor as ***an agonist, partial agonist, or inverse agonist of said receptor***". However, it is unclear how an agonist, partial agonist, or inverse agonist of said receptor is determined and correlated to the preamble.

Applicants argue that the terms "agonist", "partial agonist", and "inverse agonist" are art recognized terms with well defined meaning, one of skill in the art would have no trouble understandering how they can be detemined. This is not persuasive because the steps

of the methods do not necessarily achieve the goal set forth in the claim preamble. Claims recite "identifying the compound or compounds that inhibit or stimulate said receptor as an agonist, partial agonist, or inverse agonist of said receptor". However, it is unclear how an agonist, partial agonist, or inverse agonist of said receptor is determined and correlated to the preamble. Since the polypeptide of SEQ ID NO: 20 is an orphan GPCR and its ligand is unknown, the methods of claims 5-8 and 28-30 cannot be used to measure the ability of a compound that inhibits the receptor. Moreover, a compound that inhibits the receptor cannot be an agonist of the receptor.

(3). Claims 28-30 recite "an endogenous version". Since neither the specification nor the prior art defines the term unambiguously, the claims are indefinite.

Applicants refers to page 5 of the specification for the term "endogenous" and argue that one of skill in the art would recognize that the endogenous receptors recited in the rejected claims are receptors that are naturally produced. This is not found to be persuasive because the specification provides no characteristic features and thus an unambiguous definition for "an endogenous version" of the polypeptide of SEQ ID NO: 20.

(4). Claims 28-30 are indefinite because they recite "stringent conditions", however, only the washing conditions are given, leaving the hybridization conditions undefined.

Applicants argue that the meaning of the phrase in question would be well known by one of skill in the art. This is not persuasive because only the washing conditions are given, leaving the hybridization conditions undefined. Since neither the specification nor the prior art defines the term unambiguously, the claims are indefinite.

Conclusion

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

Ruixiang Li

Ruixiang Li, Ph.D.
Primary Examiner
October 9, 2007

RUIXIANG LI, PH.D.
PRIMARY EXAMINER